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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/740,075	12/17/2003	Perry F. Renshaw	04843/117002	1400

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EXAMINER	
FEDOWITZ, MATTHEW L	
ART UNIT	PAPER NUMBER
1623	

DATE MAILED: 09/12/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/740,075	RENSHAW ET AL.	
	Examiner	Art Unit	
	Matthew L. Fedowitz	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 June 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed June 20, 2005 has been received, entered and carefully considered. The amendment affects the instant application accordingly:

A. Claims 8 and 15 have been amended.

B. Claims 19 and 20 are new.

C. Comments regarding the Office Action have been provided drawn to:

1. Applicant's comments regarding the claim rejections under 35 U.S.C. §103 have been considered and are persuasive in part.

2. Applicant's comments regarding the claim rejections under 35 U.S.C. §112 Second Paragraph have been considered and are persuasive in part.

D. Claims 1-20 are pending in this action.

Claim Rejections - 35 USC § 112 Second Paragraph

Applicant's arguments in regard to the §112 Second Paragraph rejections in the office action dated December 16, 2004 are found to be persuasive.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action. Claim 14 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The applicant states that the substance abuse disorders are alcohol, caffeine or cocaine usage. The use of these substances is not considered to be a disorder and this claim is considered to be indefinite. For examination purposes the dependence on such substances will be considered to be the disorder.

Claim Rejections - 35 USC § 103

Applicant's arguments obviate the §103 rejection in the office action dated December 16, 2004 in regard to claims 1-3, 12 and 17. However, the applicant's arguments are not found to be persuasive in regard to claims 4-7, 16 and 18. The reason applicant's arguments are not persuasive is because the sleep normalizing effects are due to the choline component of the composition in the method claims. The effects of this component are taught in the prior art and are discussed in the office action dated December 16, 2004 where on page 3 of the Greenwell article it states that the effects of choline has been compared to CDP-choline to determine whether cognitive function has been increased. One skilled in the art would find this article suggestive of the fact that CDP-choline is effective for increasing cognitive function as well as the other functions discussed for choline alone that include inducing and maintaining sleep.

As noted above, a further search of the prior art reveals additional obviousness rejections that must be made. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1-3, 12 and 17 rejected under 35 U.S.C. 103(a) as being unpatentable over Yamato et al, Pischel et al. and Monti et al.

Claim 1 is directed to a method of normalizing the sleep wake by administering a therapeutically effective amount of a cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound and an adenosine elevating compound to a mammal to normalize the sleep/wake cycle. Claim 2 narrows claim 1 to where the administration reduces fatigue, tiredness, increases wakefulness, or improves sleep quality. Claim 3 narrows claim 1 to cytidine-

containing compounds to cytidine. Claim 4 narrows claim 1 to where the cytidine-containing compound is choline. Claim 12 is directed to a method of treating a sleep disorder by administering a therapeutically effective amount of a cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound and an adenosine elevating compound. Claim 17 is directed to a method of increasing cognitive function by administering a therapeutically effective amount of a cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound and an adenosine elevating compound.

Yamamoto et al. teach that uridine and cytidine induce sleep (see column 3 line 30 – column 4 line 4 and claims 1-5). Yamamoto et al. does not teach the use of creatine or adenosine to induce sleep

However, Pischel et al. teach that creatine provides a deeper and more relaxing sleep (see column 4 line 40-line 53). And Monti et al. teach that Adenosine modulates sleep in Rats as an animal model for humans (see entire article).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to combine the teachings above to claim the methods as in the instant application. All of the compounds, which are substituted in the instant application, are taught in the art, and the compounds are known to have sleep inducing properties. Obviousness based on similarity of structure and function entails motivation to claim the methods as the applicant has in expectation that similar compounds will have similar properties; therefore, one of ordinary skill in the art would be motivated to claim the methods as the applicant has in searching for new mean to apply cytidine, cytosine, uridine, creatine and adenosine containing compounds.

Claim Rejections - 35 USC § 112 First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 8-15, 17 and 19-20 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for those specific cytidine, cytosine, uridine, creatine and adenosine containing compounds described, does not reasonably provide enablement for every compound that contains cytidine, cytosine, uridine, creatine and adenosine. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

The determination that "undue experimentation" would have been needed to make and use the claimed invention is not a single, simple factual determination. Rather, it is a conclusion reached by weighing all the factual considerations. In re Wands, 8 USPQ2d 1400 (CAFC). There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include but are not limited to:

1. The breadth of the claims;

2. The nature of the invention;

3. The state of the prior art;

4. The level of one of ordinary skill;

5. The level of predictability in the art;

6. The amount of direction provided by the inventor;

7. The existence of working examples; and

8. The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

Wands Analysis

1. The Breadth of the Claims.

The breadth of the instant claims are seen to encompass a method of normalizing the sleep/wake cycle by administering a therapeutically effective amount of a cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound and an adenosine elevating compound to a mammal to normalize the sleep/wake cycle; wherein the administration reduces fatigue, tiredness, increases wakefulness, or improves sleep quality; wherein the cytidine-containing compounds contain cytidine; wherein the compounds are chronically administered; wherein the compounds are administered to mammals, children or adolescents or older adults.

The breadth of the instant claims are also seen to encompass a method of treating a sleep disorder by administering a therapeutically effective amount of a cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound and an adenosine elevating compound; wherein the sleep disorder is caused by a substance abuse disorder such as alcohol, caffeine, or cocaine dependence; wherein the sleep disorders are insomnia, constructive or obstructive sleep apnea, restless leg syndrome, periodic limb movements, problem sleepiness or narcolepsy.

The breadth of the instant claims are also seen to encompass a method of increasing cognitive function by administering a therapeutically effective amount of a cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound and an adenosine elevating compound;

wherein the sleep disorder is not caused by a substance abuse disorder and the disorder is problem sleepiness.

Therefore the claims are seen to encompass any source of the compounds listed above whether they are from nutritional supplements or food sources consumed on a daily basis.

2. The Nature of the Invention.

The nature of the invention relates to a method of normalizing the sleep/wake, a method of treating a sleep disorder and a method of increasing cognitive function by administering a therapeutically effective amount of a cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound and an adenosine elevating compound. The invention is seen to broadly encompass any compound that contains cytidine, cytosine, uridine, creatine, and adenosine.

3. The State of the Prior Art.

The applicant discloses references to example to demonstrate broadly that cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compounds have the ability to normalize the sleep/wake cycle, treat a sleep disorder and increase cognitive function. The references then specifically point to preferred compounds such as CDP-choline, S-adenosylmethionine and triacetyl uridine. These examples however, do not demonstrate that the administration of every cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compound will normalize the sleep/wake cycle, treat a sleep disorder and increase cognitive function As a result of this finding and the lack of adequate guidance or representations in the specification, the applicant has not enabled this aspect of the claimed methods broadly. The skilled artisan in this field would not

accept the representations set forth in the instant disclosure as sufficient to enable methods for using cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compounds broadly to normalize the sleep/wake cycle, treat a sleep disorder and increase cognitive function.

4. The Level of Ordinary Skill

The level of skill is that of one with a doctoral understanding of therapeutics.

5. The Level of Predictability in the Art

The number of cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compounds varies widely, for example, these compounds can be found in nutritional supplements as well as food sources that are consumed on a daily basis. Also, the bioavailability of these compounds from the sources above is highly unpredictable as one cannot be certain that the administration of the compounds will normalize sleep or increase cognitive function. As a result, it is an uncertain science to say that any compound that may contain cytidine, cytosine, uridine, creatine or adenosine will yield a normalized sleep/wake cycle, treatment of a sleep disorder or increase cognitive function.

6. The Amount of Direction Provided by the Inventor

The applicant has not demonstrated sufficient guidance provided in the form of adequate supporting representations or art recognized correlations in patent or non-patent literature. For example, the applicant only discloses references to examples of how cytidine-, cytosine-, uridine-, creatine-, adenosine-containing compounds are believed to normalize the sleep/wake

cycle, treat a sleep disorder and increase cognitive function. This does not enable one to claim any compound containing cytidine, cytosine, uridine, creatine or adenosine to have the ability to normalize the sleep/wake cycle, treat a sleep disorder and increase cognitive function.

7. The Existence of Working Examples

A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright, 27 USPQ2d 1510 (CAFC). The disclosure does not demonstrate sufficient evidence to support the applicant's claim to make and use any compound that contains cytidine, cytosine, uridine, creatine or adenosine to have the ability to normalize the sleep/wake cycle, treat a sleep disorder and increase cognitive function. Applicant's broad claims necessarily require a broad disclosure or guidance in the art to accept the methods of using compounds containing cytidine, cytosine, uridine, creatine or adenosine commensurate in scope with the instant claims.

8. The Quantity of Experimentation Needed to Make or Use the Invention Based on the Content of the Disclosure

In order for any compound containing cytidine, cytosine, uridine, creatine or adenosine to have the ability to normalize the sleep/wake cycle, treat a sleep disorder and increase cognitive function, it would be necessary to demonstrate how the vast number of compounds that contain the amino acids above would all provide the outcome as claimed by the applicant by providing

references that contain directions or examples. The specification submitted and examples therein do not demonstrate this broadly. Therefore, one of ordinary skill in the art would require a significant amount of experimentation in order to use any compound containing cytidine, cytosine, uridine, creatine or adenosine to normalize the sleep/wake cycle, treat a sleep disorder and increase cognitive function.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Matthew L. Fedowitz whose telephone number is (571) 272-3105. If attempts to reach the examiner by telephone are unsuccessful, the examiner's primary, James O. Wilson, can be reached on (571) 272-0661. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Matthew L. Fedowitz, Pharm.D., Esq.

James O. Wilson, Supervisory Patent Examiner
Art Unit 1623